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Health-related quality of life among children with mental disorders: A systematic review

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Abstract

Purpose: To systematically review studies about the quality of life (QOL) of children with various mental disorders relative to healthy controls and to describe limitations in these studies. **Methods:** Relevant articles were searched using different databases, by checking reference lists and contacting experts. We included articles that either compared children with mental disorders to healthy controls/norm values or made such a comparison possible.

Results: Sixteen out of 4,560 articles met the pre-defined inclusion criteria. These studies revealed that the QOL of children with various mental disorders is compromised across multiple domains. The largest effect sizes were found for psychosocial and family-related domains and for the total QOL score, whereas physical domains generally were less affected. The most important limitations in the existing literature include the lack of study samples drawn from the general population, the failure to use self-ratings, not considering item overlap between measuring QOL and assessing for the presence of a particular mental disorder, and not determining whether the children were receiving medication for their mental disorder.

Conclusions: Children with mental disorders experience a considerable reduction in QOL across various domains. Research studies that avoid previous limitations are crucial to fill existing knowledge gaps.

Keywords: health-related quality of life, mental disorder, children, systematic review

Abbreviations:

ADHD: Attention-deficit/hyperactivity disorder

ASD: Autism spectrum disorders

CHIP: Child Health and Illness Profile

CI: Confidence interval

CHQ: Child Health Questionnaire

DSM-IV-TR: Diagnostic and Statistical Manual of Mental Disorders

DUX-25: Dutch-Child-AZL-TNO-Quality-of-Life

ES: Effect sizes

HRQOL: Health-related quality of life

ICD-10: International Classification of Disease and Related Health Problems

KINDL-R: Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescent - Revised Version

PedsQL: Pediatric Quality of Life Inventory

SD: Standard deviation

SpLD: Specific learning disabilities

TACQOL: TNO-AZL-Child-Quality-Of-Life

QOL: Quality of life

WHO: World Health Organization

Introduction

The World Health Organization (WHO) [1] claims that *mental disorders* are a neglected field relative to *physical disorders*. To achieve a better balance between the scientific and public attention that mental and physical disorders receive, it is reasonable to use this dualistic distinction. Consequently, in this article, we build upon the frequently used definition of the ‘*International Classification of Disease and Related Health Problems*’ (ICD-10) [2] and apply the thereby-constructed distinction between mental and physical disorders as an analytic framework. According to the ICD-10 definition, mental disorders are the “*existence of a clinically recognisable set of symptoms or behaviours associated in most cases with distress and interference with personal functions* [2].” In line with this definition, disorders from Chapter V of the ICD-10 are covered by the term *mental disorders*, whereas all categories from the other chapters are treated as *physical disorders*. Mental disorders in the ‘*Diagnostic and Statistical Manual of Mental Disorders*’ (DSM-IV-TR [3]) are defined as in the ICD-10, and the terms are comparable between the two systems.

One possible way to analyze the impact of a specific disorder is to use the concept of ‘*health related quality of life*’ (*HRQOL*), which can be described as a subjective, multidimensional and dynamic construct that comprises physical, psychological and social functioning [4], thereby going beyond checking for the presence of specific symptoms [5]. *HRQOL* is, among other things, influenced by the characteristics of a particular disorder, and in children by the stage of the child’s development [4]. The term ‘*quality of life*’ (*QOL*) includes the same dimensions as *HRQOL*, as well as further dimensions [6]. The concept of *QOL* is not clearly separated from the *HRQOL* concept in many publications [5].

For simplicity, we will use the more commonly accepted term *HRQOL* in this article.

Different authors highlight that most of the *HRQOL* studies published to date have examined the relationship between *physical disorders* and *HRQOL* [5; 7-9]. That the relationship between *mental disorders* and *HRQOL* has not received the same degree of scientific attention can be partially explained by the methodical challenge called ‘*item overlap*’, which is bigger for mental (especially in psychosocial *HRQOL* domains) than for physical disorders [10; 11]. Item overlap exists when the *HRQOL* items, and the items utilized to assess the presence of a particular disorder are similar in

content [10; 11]. According to Katschnig [10], researchers should control for item overlap during statistical analysis.

Despite the above-mentioned challenge, some investigators have examined the impact of mental disorders on HRQOL. In studies involving *adults*, those with mental disorders consistently report lower HRQOL than healthy controls [12-14]. In general, *children* have been less frequently considered in HRQOL studies than adults [15]. However, it is important to study children separately, because certain issues are specific for this age group (e.g., the impressive progression of their physical and psychosocial development, greater degree of dependence upon adults, and the different prevalence rates and manifestations of mental disorders) [5; 16; 17].

The aims of this systematic review were twofold: first, to systematically review studies about the HRQOL of children with mental disorders versus healthy controls and second, to identify the limitations of existing articles on this topic, so as to enhance the design of future studies. We failed to find any previous systematic reviews that *concurrently* evaluated HRQOL among children with various mental disorders and met the above-mentioned aims.

METHODS

Data sources and search strategy

A literature search was conducted (up to March 2011) to identify studies that (1) compare the HRQOL of children (ages 0-18 years) with mental disorders versus healthy peers/norm values or (2) provide data that makes such a comparison feasible. The search was conducted in two steps. First, the following databases were searched: DARE, the Cochrane database of systematic reviews, CINAHL, Embase, PsychInfo, PsyIndex, Pubmed, NDLDT and ProQuest. Searches were mainly conducted in English, using the following keywords and Boolean operators: (child* OR adolescent* OR 'school' OR 'p(a)ediatric' OR 'youth') AND (psychology* OR 'psychic' OR psychiatr* OR 'mental health' OR 'mental disorder' OR emotional OR behavio(u)ral OR developmental OR 'mood disorder') AND ('Quality of life' OR QOL OR well-being). Some additional databases were searched in German (e.g.,

databases with German dissertations). Second, the reference lists of relevant articles and book chapters were consulted for additional materials. Experts in this research field were asked whether they had knowledge of any published or unpublished studies about HRQOL in children with mental disorders.

Study selection

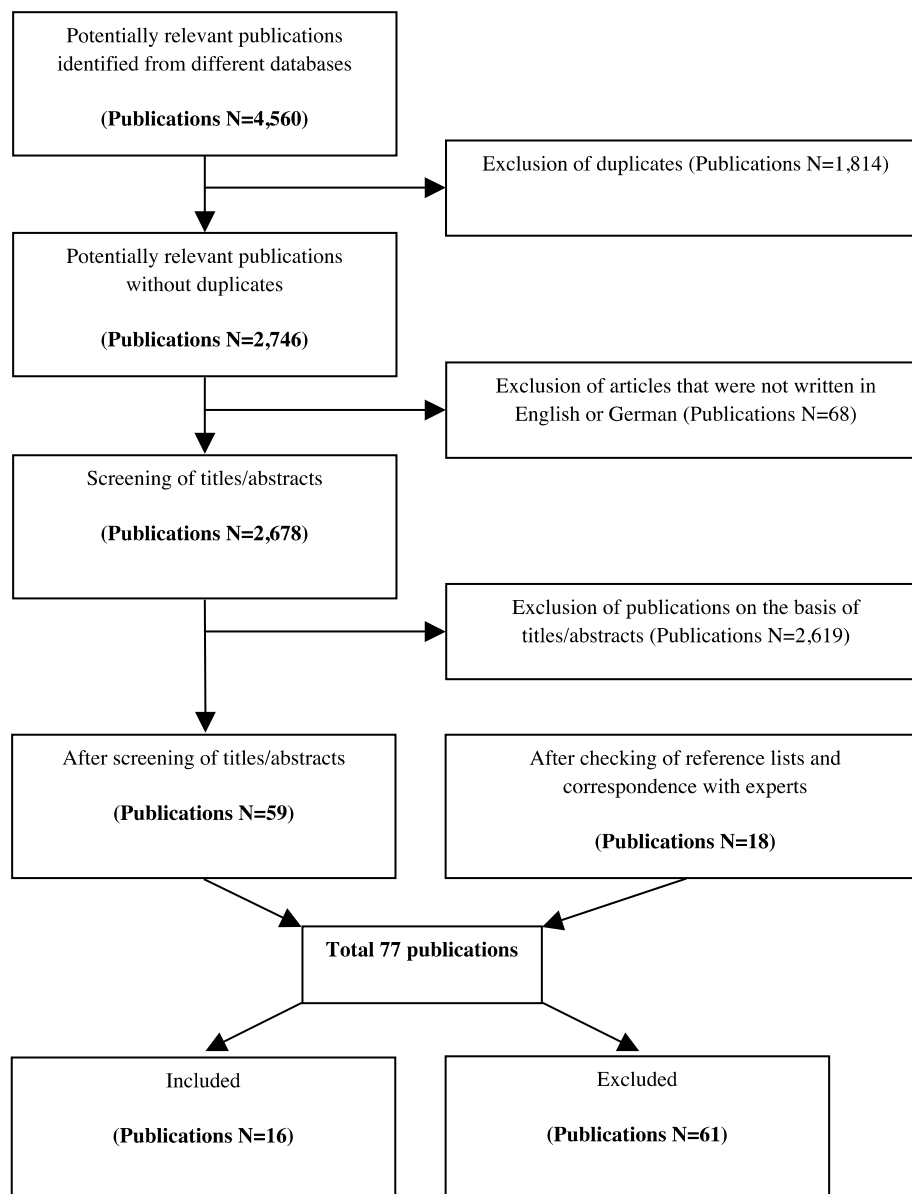
The process of study selection is outlined in Figure 2.1. The first search step revealed 4,560 articles. After eliminating all duplicates (1,814) and those articles not written in English or German (68), 2,678 articles remained. The titles and abstracts of these articles were screened for eligibility by the first author (M.D.). Articles were excluded if at least one of the exclusion criteria was met (see below). Altogether, 2,619 articles were excluded, based upon their title or abstract. The second search step resulted in an additional 18 articles. Full texts of these 18 articles and those articles identified in the databases and not yet excluded (59 articles; for a total of 77 articles) were obtained and reviewed independently by two authors (M.D. and M.A.L.). Papers were excluded if at least one of the following pre-defined criteria was met:

1. Only published as an abstract or poster/no (quantitative) empirical data
2. Data already published in another (included) article
3. Description of mental health and HRQOL of children with physical disorders
4. No disorder from Chapter V of the ICD-10 or DSM-IV-TR
5. Mental disorder diagnosis not confirmed (not diagnosed through a specialist or assessed using a standardized, validated instrument based on ICD or DSM criteria)
6. No standardized HRQOL measure
7. Participants older than 18 years
8. No comparison versus healthy controls/norm values or only a rudimentarily described comparison (if articles did not directly address the differences between children with mental disorders and healthy controls/norms, but provided all the data necessary for this comparison, the article was included)

9. A pharmaceutical study without baseline data
10. More than half of the children with mental disorders were on psychotropic medication during the timeframe to which the HRQOL assessment referred (this criterion was introduced to exclude medical treatment as a potential confounder)
11. Medication unknown and more than half of the children with mental disorders were likely on medication (e.g., children treated in a psychiatric clinic)
12. No descriptive statistics (group means, SD and *N*) reported, computable or provided (to potentially resolve this deficiency, authors were contacted repeatedly and were asked to send us the data)
13. Insufficient quality of reporting (this criterion was applied when multiple concurrent details that normally are reported – like sampling methods, participant details, and statistical analysis methods – were missing).

Inclusion criteria were defined complementary to the exclusion criteria. Disagreements in the appraisal of the articles between M.D. and M.A.L. were resolved through discussion. Ultimately, sixteen publications were included, while 61 were excluded. The reasons for exclusion are described in the Results section.

Figure 2.1: Study selection



Data extraction and synthesis

Two independent reviewers (M.D. and M.M.K.) extracted data from the 16 studies. If crucial information was missing or ambiguous, we asked the authors to send us the missing data or clarify any ambiguity. Concerning study group sizes, we always reported the largest N for which HRQOL data were provided. In accordance with Cohen [18], effect sizes (ES) were calculated to evaluate the magnitude of the differences between children with mental disorders and healthy controls/norms. ES also were calculated for studies for which ES were calculated in the reporting paper, because different formulas exist. Each ES was interpreted as *small* (0.2), *medium* (0.5) or *large* (0.8) in magnitude [18]. $ES \geq 0.5$ were considered *clinically meaningful*. This cut-off was defined according to the recommendation for HRQOL research [19]: It is suggested that a difference of approximately *half a standard deviation (SD)* represents a ‘clinically meaningful difference’. Such a difference between the means of children with mental disorders and healthy controls would approximately lead to the here-used cut-off ‘ $ES = 0.5$ ’, given the condition that both groups have about the same SD. Furthermore, 95% confidence intervals (CI) were calculated for the ES. Because the included studies differed in relevant characteristics (e.g., specific mental disorders, age range, HRQOL measure), the ES of individual studies were not summarized using meta-analytic methods.

RESULTS

Reasons for exclusion

Reasons for exclusion are listed in Table 2.1. The most common reason for exclusion was the absence or incomplete description of comparisons.

Table 2.1: Reasons for exclusion of articles

Reason for exclusion	Frequency
No or only rudimentarily described comparisons	16
More than half of the children with mental disorders were on psychotropic medication	11
Medication unknown and more than half of the children with mental disorders were likely on medication	6
Only abstract or poster / no (quantitative) empirical data	5
Mental disorder diagnosis non-confirmed	5
Data already published in another (included) article	4
Participants older than 18 years	4
No descriptive statistics reported, computable or provided	5
Description of mental health and HRQOL of children with physical disorders (or of a group of children that concurrently included children with mental and physical disorders)	3
No standardized HRQOL measure	1
Insufficient quality of reporting	1

Comparing the HRQOL of children with mental disorders versus controls/norms

The 16 studies included in analysis are summarized in Table 2.2. ES are organized by size, with the ES of the total HRQOL score (**bold and italic**) reported first, followed by the ES of higher-order HRQOL scales (**bold**) and then the different subscales. $ES \geq 0.5$ are underlined because they are considered to be clinically relevant [20]. An overview about the HRQOL measurements that were used in the included studies is provided in Table 2.3.

Table 2.2: Health-related quality of life in children with mental disorders versus healthy controls/norm values (in 16 studies that met final inclusion criteria)

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
Attention-deficit/hyperactivity disorder (ADHD)								
Escobar et al. [21]	Clinical	6 to 12	ADHD (120) versus healthy controls (120)	CHQ-PF50	Parent	For most CHQ subscales, children with ADHD had significantly lower scores than healthy children, especially for psychosocial and family-related subscales. In contrast, no significant differences were found in more physical subscales. Both summary scores were significantly lower in children with ADHD than in healthy peers	<u>PsS: -2.25 (-2.57, -1.92); PhS: -0.67 (-0.93, -0.41)</u> <u>BE: -1.98 (-2.29, -1.67); PE: -1.69 (-1.99, -1.40);</u> <u>FA: -1.42 (-1.70, -1.14); RP: -1.38 (-1.66, -1.10);</u> <u>REB: -1.23 (-1.51, -0.96);</u> <u>MH: -1.23 (-1.50, -0.95); SE: -1.09 (-1.36, -0.82);</u> <u>PT: -0.78 (-1.04, -0.52); FC: -0.53 (-0.79, -0.27);</u> <u>PF: -0.30 (-0.56, -0.05); BP: -0.21 (-0.46, 0.05);</u> <u>GH: -0.18 (-0.43, 0.08)</u>	
Klassen et al. [22]	Clinical	10 to 17	ADHD (58) versus norms (parents: 5414; children: 2361)	CHQ-PF50 & CHQ-CF87	Parent & Child	Parental rating: Parents of children with ADHD rated the family and psychosocial subscales of HRQOL as substantially reduced, whereas no differences were found in subscales with a stronger relationship to physical health. Child self-rating: Children with ADHD reported reduced HRQOL for only 3 of 9 subscales ('physical function', 'behavior', 'family activities')	<u>BE: -1.85 (-2.11, -1.59); FA: -1.61 (-1.87, -1.34);</u> <u>FC: -1.61 (-1.87, -1.34); SE: -1.05 (-1.31, -0.79);</u> <u>MH: -1.01 (-1.27, -0.75); GH: -0.18 (-0.44, 0.08);</u> <u>BP: -0.03 (-0.29, 0.23); RP: 0.05 (-0.21, 0.31);</u> <u>PF: 0.06 (-0.20, 0.32)</u>	<u>FA: -0.56 (-0.82, -0.30); BE: -0.39 (-0.65, -0.13);</u> <u>PF: -0.37 (-0.63, -0.11); RP: -0.21 (-0.47, 0.05);</u> <u>FC: -0.19 (-0.45, 0.07); MH: -0.04 (-0.30, 0.22);</u> <u>SE: 0.16 (-0.10, 0.42); GH: 0.17 (-0.09, 0.43);</u> <u>BP: 0.20 (-0.06, 0.46)</u>
Matza et al. [23]	Clinical	8 to 17	ADHD (297) versus norms (391)	CHQ-PF50	Parent	Generally, the CHQ-scores of the ADHD group were reduced for the different psychosocial (sub)scores more than for physical (sub)scales. The baseline mean 'psychosocial summary score' was reduced > 1.5 SD relative to the norm	<u>PsS: -1.56 (-1.73, -1.39); PhS: 0.70 (0.54, 0.85)</u> <u>BE: -1.81 (-1.98, -1.63); FA: -1.77 (-1.95, -1.59);</u> <u>PE: -1.72 (-1.90, -1.55); REB: -1.03 (-1.19, -0.87);</u> <u>PT: -1.00 (-1.16, -0.84); SE: -0.83 (-0.99, -0.67);</u> <u>MH: -0.57 (-0.72, -0.41); FC: -0.44 (-0.60, -0.29);</u> <u>RP: 0.02 (-0.13, 0.17); PF: 0.11 (-0.04, 0.27);</u> <u>BP: 0.20 (0.04, 0.35); GH: 0.37 (0.22, 0.52)</u>	
Rentz et al. [24]	Clinical	6 to 18	ADHD (921) versus norms (391)	CHQ-PF50	Parent	Relative to norm values, all psychosocial subscale scores and the 'psychosocial summary score' were significantly reduced in the ADHD group, while the means for the ADHD sample were mostly higher than the norms for physical subscales	<u>PsS: -1.79 (-1.93, -1.65); PhS: 0.35 (0.23, 0.47)</u> <u>PE: -1.87 (-2.01, -1.73); FA: -1.67 (-1.81, -1.54);</u> <u>BE: -1.65 (-1.79, -1.52);</u> <u>REB: -1.13 (-1.25, -1.00); SE: -0.99 (-1.11, -0.86);</u> <u>PT: -0.94 (-1.06, -0.81); MH: -0.74 (-0.86, -0.61);</u> <u>FC: -0.50 (-0.62, -0.38); RP: -0.01 (-0.13, 0.11);</u> <u>PF: 0.04 (-0.08, 0.16); BP: 0.06 (-0.06, 0.18);</u> <u>GH: 0.33 (0.21, 0.45)</u>	

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
Sawyer et al. [25]	Non-clinical	6 to 17	ADHD (308) versus no disorder (2507)	CHQ-PF50	Parent	Comparing children with ADHD versus healthy children, large ES were found for the subscales 'behavior', 'parent impact-emotional', 'family activities' and 'parent impact-time'. The smallest ES were identified for subscales with a more physical context	<u>BE: -1.64 (-1.76, -1.51); PE: -1.30 (-1.42, -1.17);</u> <u>FA: -1.15 (-1.27, -1.02); PT: -0.90 (-1.02, -0.78);</u> <u>REB: -0.77 (-0.89, -0.65);</u> <u>MH: -0.73 (-0.85, -0.61); SE: -0.64 (-0.76, -0.52);</u> <u>GH: -0.29 (-0.41, -0.17); BP: -0.29 (-0.41, -0.18);</u> <u>RP: -0.21 (-0.33, -0.09); PF: -0.19 (-0.31, -0.07)</u>	
Jafari et al. [26]	Clinical	8 to 17	ADHD (72) versus healthy controls (140)	PedsQL 4.0 generic core scale (23 item)	Parent & Child	Parents of children with ADHD and the children with ADHD themselves reported reduced HRQOL values for all (sub)scales and the total HRQOL score	<u>Total: -1.01 (-1.31, -0.71)</u> <u>PsS: -1.05 (-1.35, -0.75); PhS: -0.64 (-0.93, -0.35)</u> <u>sch: -1.14 (-1.45, -0.84); emo: -0.97 (-1.27, -0.67);</u> <u>soc: -0.42 (-0.71, -0.14)</u>	<u>Total: -1.12 (-1.42, -0.82)</u> <u>PsS: -1.09 (-1.39, -0.79); PhS: -0.78 (-1.08, -0.49)</u> <u>sch: -0.95 (-1.25, -0.65); soc: -0.91 (-1.21, -0.61);</u> <u>emo: -0.64 (-0.93, -0.35)</u>
Pongwilairat et al. [27]	Clinical	8 to 12	ADHD (46) versus healthy controls (94)	PedsQL 4.0 generic core scale (23 item)	Parent & Child	Parental ratings: The total HRQOL score and all of the psychosocial HRQOL (sub)scales were significantly compromised in children with ADHD versus healthy controls, whereas no differences were found for 'physical health summary score'. Child self-ratings: The total HRQOL score, 'physical health' and all psychosocial HRQOL (sub)scales were significantly reduced in the ADHD group versus controls	<u>Total: -0.73 (-1.09, -0.36)</u> <u>PsS: -0.98 (-1.36, -0.61); PhS: -0.26 (-0.61, 0.09)</u> <u>scho: -1.10 (-1.47, -0.72);</u> <u>emo: -0.67 (-1.03, -0.31); soc: -0.67 (-1.03, -0.30)</u>	<u>Total: -0.85 (-1.22, -0.49)</u> <u>PsS: -1.08 (-1.46, -0.71); PhS: -0.37 (-0.73, -0.02)</u> <u>scho: -1.18 (-1.56, -0.80); soc: -0.80 (-1.17, -0.44);</u> <u>emo: -0.71 (-1.07, -0.34);</u>
Preuss et al. [28]	Clinical	6 to 18	ADHD (1478) versus norms (1708)	CHIP-CE	Parent	According to parent ratings, HRQOL means of the ADHD group were considerably reduced versus a healthy control group for all subscales (ADHD sample scores averaged two SD below the means for healthy controls)	<u>ach: -1.92 (-2.00, -1.83); ra: -1.70 (-1.78, -1.62);</u> <u>sat: -1.41 (-1.48, -1.33); res: -1.26 (-1.34, -1.19);</u> <u>com: -0.73 (-0.80, -0.66)</u>	

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
ADHD and additional disorders								
Flapper et al. [29]	Clinical	7 to 10	Development coordination disorder combined with ADHD (23) versus healthy controls (23)	DUX-25; TAC-QOL	Parent & Child	DUX-25: Parental ratings: All HRQOL subscales and the total HRQOL score were significantly lower for the clinical group versus healthy controls. Child self-ratings: Two of the HRQOL subscales ('emotional' and 'social') and the total HRQOL score also were significantly lower TACQOL: Parental ratings: All but one HRQOL subscale ('bodily functioning') and the total HRQOL score were significantly reduced in ADHD children versus healthy controls. Child self-ratings: All but two HRQOL subscales ('bodily functioning' and 'negative moods') and the total HRQOL score were significantly lower in children with ADHD	DUX-25: <u>total: -1.06 (-1.68, -0.44)</u> <u>home: -1.01 (-1.63, -0.40);</u> <u>phy: -0.97 (-1.58, -0.36);</u> <u>emo: -0.87 (-1.47, -0.26);</u> soc: -0.46 (-1.04, 0.13) TACQOL: <u>total: -1.52 (-2.18, -0.87)</u> <u>SF: -1.78 (-2.46, -1.10);</u> MF: -1.46 (-2.11, -0.81); <u>AF: -1.12 (-1.74, -0.49);</u> NM: -1.11 (-1.73, -0.49); <u>CF: -0.99 (-1.60, -0.38);</u> PM: -0.85 (-1.45, -0.24); BF: -0.31 (-0.89, 0.27)	DUX-25: <u>total: -1.11 (-1.73, -0.49)</u> <u>emo: -1.87 (-2.56, -1.18);</u> soc: -0.76 (-1.36, -0.16); <u>phy: -0.56 (-1.15, 0.03);</u> home: -0.07 (-0.65, 0.51) TACQOL: <u>total: -1.35 (-1.99, -0.71)</u> <u>AF: -1.37 (-2.01, -0.73);</u> SF: -1.33 (-1.97, -0.69); <u>CF: -1.16 (-1.78, -0.53);</u> PM: -0.89 (-1.50, -0.29); <u>NM: -0.74 (-1.34, -0.14);</u> MF: -0.72 (-1.31, -0.12); BF: -0.48 (-1.07, 0.11)
Wehmeier et al. [30]	Clinical	6 to 17	ADHD with comorbid oppositional defiant or conduct disorder (180) versus norms (14836)	KINDL-R	Parent	Compared to published norms for healthy children, the ADHD group had considerably lower HRQOL scores in different domains, with large ES for 5 of 6 subscales and the total HRQOL score. The ES for the 'physical' subscale were very small	<u>Total: -1.13 (-1.27, -0.98)</u> <u>fri: -1.21 (-1.36, -1.06);</u> fam: -1.18 (-1.33, -1.04); <u>s-e: -0.92 (-1.06, -0.77);</u> scho: -0.81 (-0.95, -0.66); emo: -0.48 (-0.63, -0.34); phy: 0.06 (-0.09, 0.21)	

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
Conduct disorder								
Sawyer et al. [25]	Non-clinical sample	6 to 17	Conduct disorder (35) versus no disorder (2507)	CHQ-PF50	Parent	In 5 subscales ('behavior', 'family activities', 'parent impact-emotional', 'parent impact-time', 'role/social limitations-emotional/behavioral'), large ES were identified when children with versus children without a conduct disorder were compared. All subscales with a stronger physical component exhibited small ES	<u>BE: -2.28 (-2.62, -1.94); FA: -1.59 (-1.93, -1.26); PE: -1.09 (-1.42, -0.75); PT: -1.08 (-1.42, -0.75); REB: -0.92 (-1.25, -0.58); SE: -0.72 (-1.06, -0.39); MH: -0.62 (-0.96, -0.29); GH: -0.38 (-0.71, -0.04); RP: -0.13 (-0.47, 0.20); BP: -0.12 (-0.45, 0.22); PF: -0.01 (-0.34, 0.33)</u>	
Specific learning disabilities (SpLD)								
Rotsika et al. [31]	Clinical	8 to 14	SpLD (99) versus typically developing children (282)	KINDL-R & Kid-KINDL-R / Kiddo-KINDL-R	Parent & Child	Parental ratings: Looking at the descriptive data, HRQOL scores were always lower for the group with SpLD relative to normally developing children (largest ES: 'everyday functioning in school'), except for the 'physical' subscale. Child self-rating: The children with SpLD had lower HRQOL scores for all subscales, compared to normally developing children, with two subscales ('emotional well-being', 'relationship with the family') especially compromised	<u>scho: -1.18 (-1.42, -0.93); s-e: -0.57 (-0.80, -0.34); fam: -0.44 (-0.67, -0.21); emo: -0.34 (-0.57, -0.11); fri: -0.26 (-0.49, -0.03); phy: 0.03 (-0.20, 0.26)</u>	<u>emo: -0.51 (-0.74, -0.28); fam: -0.51 (-0.74, -0.28); scho: -0.44 (-0.67, -0.21); phy: -0.42 (-0.66, -0.19); fri: -0.39 (-0.62, -0.16); s-e: -0.26 (-0.49, -0.03)</u>
Karande et al. [20]	Clinical	7 to 17	SpLD (150) versus norms (391)	CHQ-PF50	Parent	The mean subscale and summary scores for children with newly diagnosed SpLD were lower than norm values. Clinically significant ES were discovered for 9 of 12 subscales and the two summary scores	<u>PsS: -1.33 (-1.54, -1.13); PhS: -1.08 (-1.28, -0.88)</u> <u>PE: -1.56 (-1.77, -1.35); FA: -1.54 (-1.75, -1.33); PT: -1.36 (-1.57, -1.16); BE: -1.20 (-1.40, -1.00); REB: -1.23 (-1.44, -1.03); GH: -0.96 (-1.16, -0.76); RP: -0.95 (-1.15, -0.75); PF: -0.92 (-1.12, -0.73); MH: -0.71 (-0.91, -0.52); SE: -0.46 (-0.65, -0.27); FC: -0.35 (-0.54, -0.16); BP: -0.34 (-0.53, -0.15)</u>	

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
Autism spectrum disorder (ASD)								
Kuhlthau et al. [32]	Clinical	2 to 17	ASD (286) versus norms (8714)	PedsQL 4.0 generic core scale (23 item)	Parent	Compared to published norms of healthy children, children with ASD exhibited reduced total HRQOL score and (sub)scale scores (largest ES: 'social functioning'), whereas 'physical functioning' was least compromised	Total: -1.10 (-1.22, -0.98) PsS: -1.39 (-1.51, -1.27); PhS: -0.48 (-0.60, -0.36) soc: -1.64 (-1.76, -1.52); emo: -0.90 (-1.01, -0.78); scho: -0.74 (-0.85, -0.62)	
Shipman et al. [33]	Clinical	12 to 18	ASD (39) versus norms (parents: 1629; children: 963)	PedsQL 4.0 generic core scale (23 item)	Parent & Child	Versus published norms, children with ASD and their parents reported significantly lower HRQOL for all domains (children: largest ES: 'physical functioning'; smallest ES: 'school functioning'; parents: largest ES: 'social functioning'; smallest ES: 'physical functioning')	Total: -1.43 (-1.75, -1.11) PhS: -0.71 (-1.03, -0.40) soc: -1.81 (-2.13, -1.48); emo: -1.24 (-1.56, -0.92); scho: -0.83 (-1.15, -0.51)	Total: -0.87 (-1.19, -0.55) PhS: -1.03 (-1.35, -0.71) soc: -0.76 (-1.09, -0.44); emo: -0.55 (-0.88, -0.23); scho: -0.43 (-0.75, -0.11)
Schizophrenia / schizoaffective disorder								
Stewart et al. [34]	Clinical	10 to 17	Schizo-phrenia (10) versus norms (391)	CHQ-PF50	Parent	ES reveal that schizophrenia especially affects psychosocial (sub)scales, whereas physical health is less affected (generally smaller ES). However, some physical (sub)scales still exhibited clinically-relevant ES	PsS: -3.05 (-3.71, -2.39); PhS: -0.56 (-1.19, 0.07) REB: -2.92 (-3.58, -2.26); MH: -2.45 (-3.10, -1.80); FA: -2.36 (-3.01, -1.71); PE: -2.30 (-2.95, -1.65); SE: -2.10 (-2.74, -1.45); PT: -2.00 (-2.64, -1.35); BE: -1.86 (-2.50, -1.22); PF: -1.37 (-2.01, -0.74); RP: -0.96 (-1.59, -0.33); FC: -0.38 (-1.01, 0.25); BP: -0.09 (-0.72, 0.54); GH: 0.34 (-0.28, 0.97)	
Stewart et al. [34]	Clinical	10 to 17	Schizo-affective disorder (7) versus norms (391)	CHQ-PF50	Parent	ES comparing children with schizoaffective disorders versus norm values were especially large for the 'psychosocial summary score' and for related and family-related subscales. In contrast, ES were smaller for the 'physical summary score' and related subscales	PsS: -3.07 (-3.85, -2.29); PhS: -0.09 (-0.84, 0.66) FA: -2.94 (-3.72, -2.17); REB: -2.87 (-3.65, -2.10); PE: -2.78 (-3.55, -2.00); BE: -2.22 (-2.99, -1.46); MH: -2.11 (-2.87, -1.35); SE: -1.78 (-2.54, -1.03); PT: -1.60 (-2.36, -0.85); FC: -0.83 (-1.58, -0.08); PF: -0.63 (-1.38, 0.12); BP: -0.46 (-1.21, 0.29); RP: -0.30 (-1.04, 0.45); GH: 0.74 (-0.01, 1.49)	

Study	Sample ^a	Age ^a	Comparison (N)	Measure	Rater HRQOL	Main outcomes	ES (CI lower limit, CI upper limit) parents	ES (CI lower limit, CI upper limit) children
Mood disorders								
Freeman et al. [35]	Clinical	8 to 18	Bipolar disorder (89) versus norms (6813)	KINDL-R	Parent	HRQOL (total scale score and all subscale scores) among bipolar children were lower than among healthy controls, especially for psychosocial subscales	Total: -1.96 (-2.17, -1.75) <u>fam</u> : -1.70 (-1.92, -1.49); <u>scho</u> : -1.18 (-1.39, -0.97); <u>s-e</u> : -1.33 (-1.54, -1.12); <u>fri</u> : -1.32 (-1.53, -1.10); <u>emo</u> : -1.00 (-1.21, -0.79); <u>phy</u> : -0.55 (-0.76, -0.34)	
Stewart et al. [34]	Clinical	10 to 17	Bipolar disorder I (45) versus norms (391)	CHQ-PF50	Parent	Comparing bipolar children and norm values, especially large ES are noted for psychosocial and family-related (sub)scales. For the 'physical summary score' and related subscales, the ES were much smaller, but nevertheless sometimes clinically meaningful	PsS: -3.38 (-3.76, -3.00); PhS: -0.04 (-0.35, 0.26) <u>FA</u> : -3.16 (-3.53, -2.79); <u>MH</u> : -2.72 (-3.07, -2.36); <u>REB</u> : -2.70 (-3.06, -2.34); <u>BE</u> : -2.61 (-2.96, -2.25); <u>PE</u> : -2.41 (-2.75, -2.06); <u>SE</u> : -2.08 (-2.42, -1.74); <u>PT</u> : -2.03 (-2.36, -1.69); <u>FC</u> : -1.15 (-1.46, -0.83); <u>PF</u> : -0.60 (-0.91, -0.29); <u>BP</u> : -0.53 (-0.84, -0.22); <u>RP</u> : -0.39 (-0.70, -0.08); <u>GH</u> : 0.28 (-0.03, 0.58)	
Sawyer et al. [25]	Non-clinical	6 to 17	Major depressive disorder (53) versus no disorder (2507)	CHQ-PF50	Parent	Versus healthy children, children with a major depressive disorder exhibited reduced HRQOL in different subscales, with large ES for 'mental health', 'parent impact-emotional', 'role/social limitations-emotional/behavioral', 'family activities' and 'self-esteem'	<u>MH</u> : -1.53 (-1.80, -1.25); <u>PE</u> : -1.32 (-1.60, -1.05); <u>REB</u> : -1.05 (-1.32, -0.78); <u>FA</u> : -0.99 (-1.26, -0.71); <u>SE</u> : -0.83 (-1.11, -0.56); <u>PT</u> : -0.79 (-1.06, -0.51); <u>BE</u> : -0.76 (-1.03, -0.48); <u>BP</u> : -0.72 (-0.99, -0.45); <u>GH</u> : -0.60 (-0.87, -0.32); <u>RP</u> : -0.27 (-0.54, 0); <u>PF</u> : -0.21 (-0.48, 0.06)	

Abbreviations: *ADHD*: attention-deficit/hyperactivity disorder; *ASD*: autism spectrum disorders; *SpLD*: specific learning disabilities; *CHIP*: Child Health and Illness Profile; *CHQ*: Child Health Questionnaire; *DUX-25*: Dutch-Child-AZL-TNO-Quality-of-Life; *KINDL-R*: Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescent - Revised Version; *PedsQL*: Pediatric Quality of Life Inventory; *TACQOL*: TNO-AZL-Child-Quality-Of-Life; *HRQOL*: health-related quality of life; *ES*: effect sizes; *CI*: confidence interval; Scales: **PsS**: psychosocial summary score; **PhS**: physical summary score; subscales: CHIP: ach: achievement; ra: risk avoidance; sat: satisfaction; res: resilience; com: comfort; CHQ: REB: role/social limitations-emotional/behavioral; BE: behavior; MH: mental health; SE: self-esteem; PE: parent impact-emotional; PT: parent impact-time; FA: family activities; FC: family cohesion; PF: physical functioning; RP: role/social limitations-physical; BP: bodily pain/discomfort; GH: general health perceptions; DUX-25: phy: physical; emo: emotional; soc: social; KINDL-R: fri: friends; fam: family; s-e: self-esteem; scho: school; emo: emotional well-being; phy: physical well-being; PedsQL: sch: school; emo: emotional; soc: social; TACQOL: CF: cognitive functioning; SF: social functioning; MF: motor functioning; AF: autonomic functioning; BF: bodily functioning; NM: negative moods; PM: positive moods

^a The children with mental disorders

Table 2.3: Overview of the HRQOL instruments used in the included studies

Measurement (Abbreviation) ^a /used version(s)	Total HRQOL score/scales/subscales (meaning of a positive rated HRQOL) ^b
Child Health and Illness Profile (CHIP) [36] Parent-report: <i>Child Health and Illness Profile - Child Edition (CHIP-CE) Parent-report form</i>	<u>Achievement</u> (positive assessment of the way the child performs academically and socially with peers) <u>Risk avoidance</u> (behaviors that pose a risk to one's health/development are avoided) <u>Satisfaction</u> (positive assessment of the child's health and self-esteem) <u>Resilience</u> (positive states and behaviors of the child that are likely to enhance future health) <u>Comfort</u> (no physical and emotional symptoms and limitations)
Child Health Questionnaire (CHQ) [37] Parent-report: <i>Child Health Questionnaire Parent Form 50 Questions (CHQ-PF50)</i> Child-report: <i>Child Health Questionnaire Child Form 87 Questions (CHQ-CF87)</i>	Psychosocial Health^c Physical Health^d <u>Role/social limitations-emotional/behavioral</u> (child has no limitations in school work or activities with friends as a result of emotional or behavioral problems) <u>Behavior</u> (child never exhibits aggressive, immature, delinquent behavior) <u>Mental health</u> (child feels peaceful, happy and calm all of the time) <u>Self-esteem</u> (child is very satisfied with abilities, looks, family/peer relationships and live overall) <u>Parent impact-emotional^e</u> (parent does not experience feelings of emotional worry/concern as a result of child's physical and/or psychosocial health) <u>Parent impact-time⁵</u> (parent does not experience limitations in time available for personal needs due to child's physical and/or psychosocial health) <u>Family activities</u> (the child's health never limits or interrupts family activities nor is a source of family tension) <u>Family cohesion</u> (family's ability to get along is rated 'excellent') <u>Physical functioning</u> (child performs all types of physical activities, including the most vigorous, without limitations due to health) <u>Role/social limitations-physical</u> (child has no limitations in school work or activities with friends as a result of physical health) <u>Bodily pain/discomfort</u> (child has no pain or limitations due to pain) <u>General health perceptions</u> (child's health is believed to be excellent and will continue to be so)
Dutch-Child-AZL-TNO-Quality-of-Life (DUX-25) [38]; adapted from [39] Parent- and child-report: <i>25 items questionnaire</i>	Total HRQOL score <u>Home</u> (getting along well with the parents) <u>Physical</u> (positive beliefs/feelings about the physical health; e.g., positive appraisal of his/her power of endurance) <u>Emotional</u> (positive feelings at school, in the night, at this moment) <u>Social</u> (positive feelings about friends and teachers)
Questionnaire for Measuring Health-Related Quality of Life in Children and Adolescent - Revised Version (KINDL-R) [40] Parent-report: <i>KINDL-R (8-16-years-olds)</i> Children-report: <i>Kid-KINDL-R (8-12 years)</i> <i>Kiddo-KINDL-R (13-16 years)</i>	Total HRQOL score <u>Friends</u> (getting along well with peers all the time) <u>Family</u> (getting along well with the parents and feeling fine at home all the time) <u>Self-esteem</u> (feeling well, proud of and pleased with himself/herself and having lots of good ideas all the time) <u>School</u> (enjoying and getting along well in school all the time and never worrying about the future) <u>Emotional well-being</u> (having fun all the time and never feeling listless, alone, scared or unsure of himself/herself) <u>Physical well-being</u> (never feeling ill or low in energy and never having headaches or tummy-aches)

Measurement (Abbreviation) ^a /used version(s)	Total HRQOL score/scales/subscales (meaning of a positive rated HRQOL) ^b
Pediatric Quality of Life Inventory (PedsQL) [41; 42] Parent- and child-report: <i>PedsQL 4.0 generic core scale (23 items)</i>	Total HRQOL score Psychosocial Health Summary Score^c Physical Health Summary Score^d <u>School Functioning</u> (never having problems concentrating, never forgetting things, never having trouble keeping up with schoolwork and never missing school) <u>Emotional Functioning</u> (never feeling anxious, sad, angry, worried and never having any trouble sleeping) <u>Social Functioning</u> (almost always getting along well with peers) <u>Physical Functioning^f</u> (never having any pain or aches or problems with different physical activities and almost always having a lot of energy)
TNO-AZL-Child-Quality-Of-Life (TACQOL) [43-45] Parent-report: <i>56 item TACQOL PF (parent form)</i> Child-report: <i>56 item TACQOL CF (child form)</i>	<u>Cognitive functioning</u> (never having difficulties with school requirements like paying attention, understanding schoolwork, arithmetic, reading, etc.) <u>Social functioning</u> (never having problems getting along with peers or parents) <u>Motor functioning</u> (never having difficulties with motor functioning - like standing, walking/running, playing, balancing or doing things handily and quickly) <u>Autonomic functioning</u> (never having difficulties doing specific things independently, like going to school on his/her own, going to the lavatory on his/her own, and doing hobbies on his/her own) <u>Bodily functioning</u> (never having physical complaints, like headaches, and never feeling tired, dizzy or nauseated) <u>Negative moods</u> (never having negative feelings, e.g., feeling sad, angry, jealous or anxious) <u>Positive moods</u> (often having positive feelings, e.g., feeling happy, relaxed, enthusiastic or confident)

Further details about the measurements (e.g., about additional versions) can be found elsewhere (e.g., [5; 7; 9; 39; 46])

^a only the versions that were used in the included studies (see Table 2.2) are presented in this table, even though some instruments have additional versions

^b corresponds to the used version (see column 1)

^c in Table 2.2 called 'psychosocial summary score'

^d in Table 2.2 called 'physical summary score'

^e only computable in the parent's version

^f The 'physical health summary score' contains the same items as the subscale 'physical functioning'. To simplify matters, we therefore only mention the summary score in Table 2.2.

Attention-deficit/hyperactivity disorder (ADHD)

Children with ADHD exhibited reduced HRQOL for multiple parent-rated (sub)scales, with the largest ES identified for psychosocial (e.g., ‘behavior’, ‘parent impact-emotional’, ‘parent impact-time’) and family-related (sub)scales. ES for the parents’ ratings usually were smaller for physical (sub)scales. If HRQOL was self-rated, divergent results were evident (in one study, no ES was clinically meaningful; whereas in two other studies, most if not all ES were). Regarding the specific HRQOL domains that were compromised, results similar to those observed with parental ratings were revealed, with the largest ES evident for psychosocial and family-related (sub)scales and smaller ES for most of the physical (sub)scales.

ADHD plus additional disorders

In the study in which ADHD children also had development coordination disorders, the self- and proxy-reports revealed reduced HRQOL in physical, cognitive and social subscales. In another study, the total HRQOL score and different psychosocial subscales of children with ADHD and comorbid oppositional defiant or conduct disorders were reduced.

Conduct disorders

In one study, among children with conduct disorders, all psychosocial (especially for the subscale ‘behavior’) and family-related HRQOL subscales were clinically meaningfully reduced, whereas no such reduction was apparent in physical subscales.

Specific learning disabilities (SpLD)

The two studies involving children with SpLD identified compromised HRQOL. When parents rated their child’s HRQOL, the largest ES were evident in psychosocial (e.g., ‘school’, ‘parent impact-

emotional’, ‘parent impact-time’) and family-related (sub)scales. The ES for physical (sub)scales usually were smaller, but sometimes still clinically meaningful. In self-ratings, the ES for children with SpLD were medium for two psychosocial subscales.

Autismus spectrum disorder (ASD)

In two studies, children with ASD had reduced total and subscale scores, both by self- and proxy-report. Parents rated the ‘social’ subscale as most and ‘physical health summary score’ least compromised, while children perceived that their physical health was most and ‘school’ subscale least affected.

Schizophrenia/schizoaffective disorder

Children with either schizophrenia or schizoaffective disorder exhibited reduced HRQOL, with the largest ES identified for psychosocial and family-related (sub)scales. The ES for the ‘physical summary score’ and related subscales were mostly smaller in magnitude. However, some of these ES were still medium to large.

Mood disorders

Relative to published norms, children with bipolar disorders were reported to have reduced HRQOL, an effect that was again especially pronounced for psychosocial (e.g., ‘mental health’, ‘parent impact-emotional’) and family-related (sub)scales. However, the ES were even clinically meaningful for some physical (sub)scales. A similar pattern was identified among children with major depressive disorders.

Limitations of existing studies

Among the *included* studies, the following limitations were apparent and sometimes mentioned by the manuscript authors: First, all but one study [25] used a clinical, rather than a general population, sample. Second, only one study about ASD included children < 6 years old [32]. Third, the majority of studies (62.5%) failed to consider both parental and child HRQOL ratings, reporting only the former. Fourth, the problem of item overlap was addressed in the statistical analyses of one study only [25]. Fifth, even though item overlap sometimes was suggested as a potential explanation, other possible explanations for compromised HRQOL in children with mental disorders were sometimes not provided.

With respect to those articles that were *excluded*, the following two limitations are of special interest (see Table 2.1): First, 17 articles were excluded because more than half of the children with mental disorders were on medication during the time to which the HRQOL assessment referred, or because the medication was unknown and more than half of the children likely were receiving a psychotropic drug. Second, five articles were excluded because the particular mental disorder was not confirmed by a specialist or using a standardized, validated instrument based on ICD or DSM criteria.

DISCUSSION

This systematic review was conducted to compare the HRQOL of children with mental disorders against those of healthy controls/norm values and to describe limitations in the existing literature.

Comparing children with mental disorders versus healthy children/norm values

Parent ratings

In most of the studies and across various mental disorders, HRQOL was compromised, with ES generally large for total HRQOL scores and psychosocial and family-related (sub)scales, and less (but sometimes still clinically meaningful) for physical (sub)scales.

With regard to psychosocial domains, the largest ES usually were identified among those subscales most closely related to the particular mental disorder (e.g., ADHD and conduct disorders: ‘behavior’; SpLD: ‘school’; ASD: ‘social’; mood disorders: ‘mental health’). Some authors considered item overlapping as a possible explanation for this result [23; 25]. Furthermore, it is possible that parents may have over-emphasized the HRQOL aspect that is most closely related to the main problem their child has [31].

In addition, some of the psychosocial subscales not directly associated with the diagnostic criteria of the particular mental disorder were also compromised (e.g., ADHD: large ES in ‘self-esteem’ [21-24]) – a pattern that possibly emerged due to comorbid disorders [8; 21].

Other subscales that were compromised in various mental disorders describe the impact of the child’s mental disorder on the life of the family and parents. This pattern can be explained via different mechanisms; for instance, through parental worries about the present (e.g., meeting daily demands in school) and future (e.g., occupation potential) of their child [31]; and through parental feelings that they are to blame for their child's mental disorder [47]. Furthermore, the impact on parents could be heightened because these children need more support (e.g., doing homework), which leads to less free time for the parents, less time the parents have available for other family members, and their need for greater organizational effort to balance the child's care and parents’ work [48].

The clinically meaningful ES for physical (sub)scales that were identified in some studies [20; 21; 23; 25; 26; 29; 33-35] cannot be explained by the side effects of psychiatric drugs [49], because we excluded all studies in which more than half of the children with mental disorders were taking or were assumed to be taking psychiatric medication. However, it is possible that some of the physical (sub)scales were compromised due to comorbid physical disorders [49]. Furthermore, it must be highlighted that some items of the physical subscales had a strong relationship to specific mental disorders. For instance, one item of the ‘physical well-being’ subscale of the KINDL-R [40] asks whether the child was *tired and worn-out* – something that is also considered a typical symptom for depression.

Looking at the ES of different disorders in Table 2.2, it seems that children with schizophrenia, schizoaffective disorder and bipolar disorder experienced especially compromised HRQOL [34]. However, on closer inspection, what stands out is that the ES differ considerably between studies assessing the same mental disorder. This can be explained through methodological differences. For instance, the way that the participants were sampled seems to influence the magnitude of the ES: When the HRQOL of ADHD children was assessed using the CHQ-PF50, the ES in psychosocial and family-related HRQOL domains were mostly smaller in a study with a non-clinical sample [25] compared to other investigations that used clinical samples [21-24]. This pattern may be explained through the bias that is associated with utilizing clinical samples (see below). Beside the influence of the sampling strategy, other differences between the included studies presumably exerted some influence on the results in general and on the magnitude of the ES in particular. Thus, the differences between the used HRQOL measurements must be especially emphasized. Even though all of the generic HRQOL measurements that are described in Table 2.3 cover physical, psychological and social HRQOL domains [39], the operationalization of these superordinate domains differ across measures [39; 46]. Hence, when interpreting the results of HRQOL studies, a detailed analysis of the HRQOL measures that are used is necessary. Furthermore, it seems to be easiest to compare the impact of various mental disorders when the methods used (e.g., the sampling protocol and HRQOL measurement) are identical for each mental disorder. This requirement generally is fulfilled in studies that concurrently targeted various mental disorders. Such investigations found that, in terms of overall HRQOL, only a few differences between the distinctive mental disorders emerge, but that each mental disorder is associated with a specific pattern of reduced HRQOL subscales, as described previously [25; 50]. The few differences that were identified in the overall HRQOL between various mental disorders may be attributed to the fact that not only the mental disorders themselves, but also other factors (e.g., symptom severity) exert considerable influence on HRQOL [50].

With regard to all the above-mentioned results, one must consider that the reduced HRQOL in children with mental disorders could also be affected by not yet discussed variables like psychosocial distress in the parents. For instance, it has been demonstrated that parental distress is negatively correlated with all parent-reported HRQOL domains of children with a physical disorder.

Furthermore, the relationship between the child's impairment and most of the proxy-reported HRQOL domains was mediated by proxy-distress [51]. Similar relationships are conceivable for proxy-reported HRQOL among children with mental disorders. Consequently, studying such relationships must be considered in subsequent investigations.

Child ratings

The limited number of studies that incorporated child self-ratings do not allow for clear conclusions regarding HRQOL. However, in some studies, a similar pattern of reduced HRQOL as for parent ratings was evident, with large ES for total HRQOL score and psychosocial (sub)scales, and smaller ES for more physical (sub)scales. In contrast, other studies revealed HRQOL (sub)scale rankings that differed between children and parents. For instance, in the study on specific learning disorders, the ES for the self-rated 'school' subscale were not clinically meaningful, whereas parents rated this subscale in such a way as to produce the largest ES [31]. The authors provide multiple explanations for this discrepancy: like parents overemphasizing their child's difficulties in school, children underestimating their target problem to prevent themselves from stressful recognition, and children adjusting to their problem so no further limitations are experienced in the HRQOL subscale that targets academic functioning.

Limitations of existing studies and recommendations for further research

As described in 'Results', the first limitation that was noticed among those studies that were *included* in analysis was that all the studies except [25] used clinical samples. This may lead to biased results, because it is possible that children who have both a mental disorder and reduced HRQOL are more likely to be referred to or treated in a clinic, compared to children with mental disorders without a marked reduction in HRQOL [25]. For example, in a recently published study, referred psychiatric

outpatients exhibited lower HRQOL scores than students with equivalent levels of emotional and behavioral problems [52]. Hence, studies that use population-based approaches should be considered to validate the results found among clinical samples. The second limitation was that only one study on ASD included children < 6 years old [32]. This can be explained partially by the fact that the disorders that were the focus of these studies generally are diagnosed after a child reaches that age. However, when a mental disorder occurs earlier and can be diagnosed reliably, HRQOL should be assessed at least with parent ratings. Third, not all authors used children's self-rating of their HRQOL. Precisely because of the subjectivity of the HRQOL construct, it should – whenever possible – also be self-rated [7]. Admittedly, the cognitive abilities of very young children, and specific characteristics of particular mental disorders (e.g., limited reading ability in children with learning disorders) may hamper such self-ratings [10; 11]. Fourth, the problem of item overlap was addressed in the statistical analyses of only one study [25]. These authors found that, even after controlling for item overlap, similar relationships between mental disorders and HRQOL were observable. Hence, although there may be some item overlap, HRQOL nevertheless provides additional information beyond the symptoms of mental disorders [5; 53]. All the same, the problem of item overlap warrants further evaluation [5]. Fifth, even though item overlap sometimes was suggested as a potential explanation for reduced HRQOL scores, other possible explanations for compromised HRQOL ratings were provided by only certain authors. Subsequent articles should, therefore, address the mechanisms through which HRQOL ratings become compromised in children with mental disorders in greater detail. Hereby, other influential factors must be taken into account (e.g., the distress of parents when they rate the HRQOL of their child or the severity of the mental disorder).

With respect to those papers that were *excluded*, the first notable limitation was that many studies failed to assess the number of children receiving psychotropic medication that could influence HRQOL [11]. Second, the diagnosis of mental disorder often was not confirmed, investigators relying entirely on parental reports. Some of these studies [54] used population-based samples, which often makes diagnosis confirmation too time- and cost-consuming. However, such a population-based approach has other advantages, as in avoiding the biases that can occur when clinical samples are

used. Therefore, depending upon the aims of a particular study, one must evaluate which sampling procedure is most appropriate.

Limitations of our study

The ES presented in Table 2.2 should be interpreted with caution. These values should be treated as approximate values, because some studies used only a small sample size of children with mental disorders. Therefore, 95% CI's obtained from these studies were extremely large. Furthermore, it must be kept in mind that the analyzed studies varied methodologically, thereby reducing their comparability. Studies also used specific inclusion and exclusion criteria that could limit the generalizability of our results. Lastly, we were primarily interested to provide a baseline for the comparison of healthy children and children with mental disorders that were not on psychotropic medication (see exclusion criteria). However, a supplementary systematic review should evaluate the differences between children with mental disorders that are on psychotropic medication from those who are not. By doing so, the inclusion of randomized controlled trials would be most appropriate.

Conclusions

Our review demonstrates that children with mental disorders experience a considerable reduction in HRQOL across various domains. These effects are not just limited to emotional, social and cognitive dimensions closely related to a specific mental disorder. Hence, reduced HRQOL cannot be attributed exclusively to item overlap. For this reason, HRQOL is a useful construct that can help to expand our knowledge regarding the impact of particular mental disorders and ameliorate clinical (e.g., by better integrating the child's perspective into the treatment plan) and public health practices (e.g., by considering and comparing the HRQOL constraints of different disorders for service planning) [5]. This said our understanding of how mental disorders influence HRQOL among children remains immature and considerable research that avoids some of the limitations of prior attempts is yet needed to fill this knowledge gap.

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